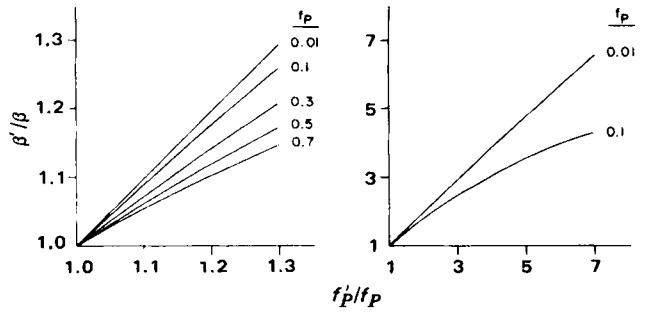

Figure 1—*Relationship between β'/β and f'_P/f_P for drugs with varying degrees of plasma protein binding.*

For the case where the binding of a drug is decreased (*i.e.*, $f'_P > f_P$), it is clear from Eq. 9 that β'/β (or $t_{1/2}/t'_{1/2}$) is smaller than f'_P/f_P but approaches f'_P/f_P as f_P approaches zero or as f'_P approaches f_P. These latter conditions apply to drugs that normally are bound to a large extent or to situations where the decrease in binding is slight.

To illustrate the relationship between relative changes in the drug half-life and plasma protein binding, Fig. 1 was constructed based on Eq. 9 using different f_P values.

From Fig. 1, it is obvious that the relationship between β'/β and f'_P/f_P is almost linear, especially when the change in f_P is relatively small. For drugs that are predominantly plasma protein bound (*e.g.*, $f_P = 0.01$), the slope of the plot is approximately one, indicating that $t_{1/2}$ is inversely proportional to f_P. Although this simple, inverse proportionality vanishes with less extensively bound drugs, the almost linear relationship between β'/β and f'_P/f_P offers a means of rapid estimation of half-life changes as a result of altered plasma protein binding.

When the percentage change in f_P is relatively large, a more rapid loss of linearity in the curves is observed with increasing f_P. Fortunately, for drugs that initially are predominantly unbound, such large percentage increases in f_P are not possible. Furthermore, the β or half-life values of these drugs are relatively insensitive to changes in binding (Fig. 1), and adjustments in the dosage regimen to correct for binding changes may not be necessary.

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BOOKS

REVIEWS

Foundations of Molecular Pharmacology, Vol. 1: Medicinal and Pharmaceutical Chemistry. By J. B. STENLAKE. The Athlone Press, University of London, Four Gower St., London WC1, England. 1979. 936 pp. 15 × 23 cm. Price $90.00.

It is easy to be enthusiastic about this well-crafted and scholarly book. The author skillfully leads us through a treatment of principles of organic chemistry applied to pharmaceutical agents. The organizational approach and its careful implementation consistently afford interesting reading.

The book is organized similar to an organic chemistry text. The medicinal agents are organized into 23 chapters by their organic chemical class; such groups as the alkanes, alkenes, benzenoid aromatic hydrocarbons, alkynes, and monohydric alcohols are included. Each chapter discusses the organic chemistry of the particular chemical class. The discussions generally are clear and succinct. The immediate pharmaceutical significance of the particular chemical property is illustrated by one or more examples from the pharmaceutical sciences. For example, following an explanation for the acidic nature of the acetylenic hydrogen atom, it is noted that the formation of a silver acetylide by the addition of silver nitrate is used as a test for identity and is the basis for the assay of some acetylenic pharmaceutical products such as ethclorvynol. Also, after a discussion of hydride reduction of aldehydes and ketones by lithium aluminum hydride and sodium borohydride, there ensues an account of the enzymatic reduction of these functional groups involving hydride donation from NADPH.

Almost all of the transitions from the general organic chemical discussion to the pharmaceutical application are made easily. Additionally, the particular pharmaceutical example usually is appropriate. One effect of this approach is to make the point repeatedly, without ever explicitly stating so, that knowledge of fundamental chemical properties is mandatory for an understanding of pharmaceutical procedures and pharmacological activities.

This reviewer has two minor criticisms relative to the author's pharmaceutical examples. There are several occasions when more appropriate pharmaceutical examples could have been presented. Also, the examples chosen could have been treated more in proportion to their importance. The following are instances in which these criticisms apply.

1. The decarboxylation of salicylic acid on bromination is discussed, but the decarboxylation of *p*-aminosalicylic acid in an acidic aqueous medium is not mentioned.
2. The structures of the amino acids GABA and taurine are given, but only GABA is cited as being an important transmitter.
3. Carbonic anhydrase-inhibiting sulfonamides are treated in detail, but benzothiazides are treated briefly.
4. The importance of ylids in synthesis is not developed.

However, these criticisms are minor, especially considering the great range of the book and the usually impressive appropriateness of the examples.

Medicinal and pharmaceutical chemists and many others in the pharmaceutical sciences should find this book to be an interesting and thought-provoking source of information. Additionally, teachers of medicinal and pharmaceutical chemistry may find that the volume is useful as a supplemental reference for both graduate and undergraduate students. Where the curriculum allows room for a course based on a format similar to that of the book (chemical class → chemical properties → pharmaceutical application), the book can serve as a textbook, although the cost is high.

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